REMARKS

Entry of this Amendment is proper under 37 C.F.R. § 1.116 because the Amendment places the application in condition for allowance for the reasons discussed herein; does not raise any new issue requiring further search and/or consideration, because the amendments amplify issues previously discussed throughout prosecution; does not present any additional claims; and places the application in better form for an appeal should an appeal be necessary. The Amendment is necessary and was not earlier presented because it is made in response to arguments raised in the final rejection. Entry of the Amendment, reexamination and further and favorable consideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.116, are thus respectfully requested.

As correctly stated in the Official Action, claims 10, 12-22, 24, 25, and 27-29 are pending in the present application. Claims 10, 12-22, 24, 25, and 27-29 stand rejected.

By the present amendment, independent claims 10, 28, and 29 have been amended to recite "treating the destruction of functional tissue." Support for this amendment can be found, at least, on page 5, lines 14 to the end of page 6. Claim 10 has been further amended to delete "chronic bronchitis." Claims 18-22 have been amended to depend from claim 28, rather than claim 17, which has been canceled. No new matter has been added. Applicants expressly reserve the right to file a continuation/divisional application on any subject matter canceled by the present amendment.

Interview Summary

Applicants gratefully acknowledge the courtesy shown by Examiner Owens to Applicants' undersigned representative in a personal interview on April 18, 2003.

During the interview the rejections under 35 U.S.C. §§ 112 and 103 were discussed. In particular, the Examiner suggested replacing the recitation of "prevention" with "treating" to overcome the rejection under 35 U.S.C. § 112, first paragraph. Additionally, Applicant's representative discussed deleting the recitation of "chronic bronchitis" from claim 10. Applicants' representative further pointed out that the severity of the diseases recited in claim 10 would not lead one skilled in the art to believe that they could be treated with a compound only known to inhibit 5- lipoxygenase.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 10, 17, 28, and 29 (and claims depending therefrom) stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter. Claim 17 has been canceled, thereby mooting this rejection as it applies to this claim. Without conceding to the merits of this rejection and solely in an effort to expedite prosecution, independent claims 10, 28, and 29 have been amended to recite "treating the destruction of functional tissue," rather than "preventing," as suggested by the Examiner in the interview of April 18, 2003. Withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 10, 12-22, 24, 25, and 27 stand rejected under 35 U.S.C. § 103 as allegedly unpatentable over Ammon et al. (EP 0 552 657) in view of Mulshine et al. (WO 95/24894) and Han (*Chin. Med. Sci. J.* 9(1):61-69). The Examiner argues that Ammon et al. recognizes that boswellic acid can be used for prophylaxis or control of inflammatory processes caused by elevated leukotriene formation. The Examiner asserts that Ammon et al. disclose the use of boswellic acid for treatment of inflammatory conditions of the joints, bronchitis, chronic hepatitis, and chronic asthma. The Examiner concludes that Ammon et al. recognize the use of boswellic acid to treat the same conditions as the presently claimed invention. Claim 17 has been canceled, thereby mooting this rejection as it applies to this claim. Claims 18-21 have been amended to depend from claim 28, which is not included in this rejection. Accordingly, the Mulshine et al. and Han publications are not discussed further here. This rejection, as it applies to independent claim 10, as amended, and claims 12-16 and 24-27, is respectfully traversed.

In order to establish a case of *prima facie* obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference or combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art reference(s) must teach or suggest all of the claim limitations. *See* M.P.E.P. §2142. Applicants respectfully submit that the cited publications do not disclose or suggest all of the claim limitations nor provide a reasonable expectation of success.

The present invention is drawn to methods of combating **severe** diseases, such as pulmonary emphysema, acute respiratory distress syndrome, shock lung, cystic fibrosis,

glomerulonephritis, and rheumatoid arthritis. The diseases to be treated by the present invention are characterized by damage to functional tissue caused by release of leucocytic elastase. The methods of the present invention comprise administering an effective amount of boswellic acid, a physiologically acceptable salt, a derivative, a salt of the derivative, a plant extract containing boswellic acid, or combinations thereof.

As noted in the specification, the inhibition of leucocytic elastase is important because during the pathophysiological processes of the diseases being treated, this enzyme (which is released from activated neutrophilic granulocytes) plays an important part in the destruction of functional tissue. Thus, the aim of the present invention is to block the final destruction of tissues and organs resulting from the indicated diseases. Until Applicants discovered that boswellic acid inhibits leucocytic elastase, it was not known that boswellic acid could be used for such a purpose.

In the prior art, 5-lipoxygenase inhibitors, such as boswellic acids, had only been claimed to be useful for treating mild to moderate diseases, such as asthma. There was no indication in the prior art that 5-lipoxygenase inhibitors could be used to treat more severe diseases, such as those treated by the present invention. Thus, there was no reasonable expectation of success.

Ammon et al. disclose the use of boswellic acid compounds for treating influencing inflammation in diseases by inhibiting leukotriene synthesis. Although Ammon et al. lists among the diseases to be treated "diseases of the joints (rheumatism)", Applicants note that rheumatoid arthritis (which is treated by the present invention) is very different from other rheumatoid diseases. Rheumatoid arthritis is based on the destruction of the articular

cartilage, in contrast to other rheumatoid diseases. This destruction leads to an irreversible deformation of the joint which hinders movement. The destruction of the articular cartilage is **not prevented** by other drugs for the treatment of rheumatoid arthritis, such as inhibitors of cyclooxygenase or 5-lipoxygenase. Thus, rheumatoid arthritis is a very different disease than rheumatism, and cannot be treated by similar drugs. Applicants further note that claim 10, as amended, does not recite any of the same diseases discussed in the Ammon et al. publication, but rather recites more serious diseases that can be treated by inhibiting human leucocytic elastase. Thus, Ammon et al. do not disclose or suggest all of the limitations of the presently claimed invention.

Thus, although Ammon et al. may disclose the use of boswellic acid for influencing inflammation, such a disclosure would not suggest the present invention, which uses boswellic acid for combating more serious diseases and conditions caused by an increase in leucocytic elastase activity.

Applicants respectfully submit that because **some** pentacyclic triterpenes were known to inhibit HLE, this is not sufficient to lead the skilled artisan to believe that all pentacyclic triterpenes do so. The Ying et al. publication cited in the specification on page 3 only tested several pentacyclic triterpenes, which were found to have a range of activity toward this enzyme; *i.e.*, some possessed poor Ki values. Applicants submit herewith, for informational purposes only, a review article (J. Patocka, *J. Appl. Biomed.* 1:7-12 (2003)) as Exhibit A. This article notes that there are **at least 4000** known triterpenes, with a wide spectrum of biological activities. *See* abstract. Thus, one skilled in the art would not

reasonably conclude that boswellic acid would inhibit HLE, nor would be motivated to select boswellic acid out of the numerous pentacyclic triterpenes known.

In summary, Ammon et al. do not disclose or suggest that the severe diseases recited in the presently claimed invention can be treated with boswellic acid. Moreover, neither Ammon et al. nor any other publication disclose or suggest that boswellic acid could be used to inhibit human leucocytic elastase. Accordingly, the cited publications do not disclose or suggest all of the claimed limitations. Withdrawal of this rejection is respectfully requested.

Conclusions

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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Attachment to REPLY & AMENDMENT dated April 29, 2003

Marked-up Claims 10, 18-22, 28, and 29

10. (Five Times Amended) A method for combating diseases selected from the group consisting of pulmonary emphysema, acute respiratory distress syndrome, shock lung, cystic fibrosis (mucoviscidosis), [chronic bronchitis,] glomerulonephritis and rheumatoid arthritis, which are caused by increased leucocytic elastase or plasmin activity or can be treated by the inhibition of normal leucocytic elastase or plasmin activity, said method comprising administering boswellic acid, a physiologically acceptable salt, a derivative, a salt of the derivative, a plant extract containing boswellic acid, or combinations thereof, in an amount effective for [preventing] treating the destruction of functional tissue, to combat said diseases to a mammalian organism in need of such combating.

18. (Amended) The method as claimed in claim [17] 28, wherein said boswellic acid is administered intraperitoneally, orally, buccally, rectally, intramuscularly, topically, subcutaneously, intraarticularly, intravenously or inhalationally.

19. (Amended) The method as claimed in claim [17] 28, wherein said boswellic acid is administered in the form of tablets, dragees, capsules, solutions, emulsions, ointments, creams, inhalants, aerosols or suppositories.

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Marked-up Claims 10, 18-22, 28, and 29

20. (Amended) The method as claimed in claim [17] 28, wherein said mammalian organism is an animal.

21. (Amended) The method as claimed in claim [17] 28, wherein said mammalian organism is a human.

22. (Amended) The method as claimed in claim [17] 28, wherein a pharmaceutical compound is also present.

28. (Amended) A method for [preventing] treating the destruction of functional tissue associated with diseases selected from the group consisting of pulmonary emphysema, acute respiratory distress syndrome, shock lung, cystic fibrosis (mucoviscidosis), chronic bronchitis, glomerulonephritis and rheumatoid arthritis, which are caused by increased leucocytic elastase or plasmin activity or can be treated by the inhibition of normal leucocytic elastase or plasmin activity, said method comprising administering boswellic acid, a physiologically acceptable salt, a derivative, a salt of the derivative, a plant extract containing boswellic acid, or combinations thereof, in an amount effective for [preventing] treating the destruction of functional tissue, to a mammalian organism in need of such prevention.

Attachment to REPLY & AMENDMENT dated April 29, 2003

Marked-up Claims 10, 18-22, 28, and 29

29. (Amended) A method for [preventing] treating the destruction of functional tissue associated with tumors and neoplasms or tumor metastases which are caused by increased plasmin activity or can be treated by the inhibition of normal leucocytic elastase or plasmin activity, said method comprising administering boswellic acid, a physiologically acceptable salt, a derivative, a salt of the derivative, a plant extract containing boswellic acid, or combinations thereof, in an amount effective for [preventing] treating the destruction of functional tissue, to a mammalian organism in need of such prevention.